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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/596,897	06/28/2006	Jason D. Bonk	C1271.70045US03	1956

23628 7590 09/11/2009

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BOSTON, MA 02210-2206

EXAMINER	
DESAI, RITA J	

ART UNIT	PAPER NUMBER
1625	

MAIL DATE	DELIVERY MODE
09/11/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/596,897	BONK ET AL.	
	Examiner	Art Unit	
	Rita J. Desai	1625	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 July 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☐ Claim(s) *2-7,10-12,14-16,18,20,21,23-28 and 35-68* is/are pending in the application.

4a) Of the above claim(s) *3,7,10,11,26-28, 35-38, 55-60, 62, 64, 66-68* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *2,4-6,12,14-16,18,20,21,23-25,39-54,61,63 and 65* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *10/18/06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Applicants have elected Group I of the restriction..

Group I claims 2, 4, 5-6, 12, 14-16, 18, 20-21, 23-25, 39-54, 61, 63, and 65, drawn to compounds of the formula Ia where RA and RB together form a six-membered carbocyclic ring, X is not interrupted by an O, and R1 and R1' are H, alkyl, alkyl aryl, cycloakyl or combined to form a morpholine or piperidine, and compositions thereof, for prosecution in the present application. Furthermore, Applicant elects the compound of Example 4 on page 100 as the species for search purposes..

Applicant's election without traverse of Group I in the reply filed on 7/15/09 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

The Restriction is made FINAL.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 2, 4, 5-6, 12, 14-16, 18, 20-21, 23-25, 39-54, 61, 63, and 65 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for R2 to be alkyl or alkyloxyalkyl, and X to be an alkyl does not reasonably provide enablement for R2 to be any such as R4, -X-R4, -X-Y-R4 and X-R5 wherein X-Y, R4 and R5 have a variety of different definitions nor for X to have all the different substitutents and variations. The specification does

not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

In re Wands, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988).

There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue". These factors include 1) the breadth of the claims, 2) the nature of the invention, 3) the state of the prior art, 4) the level of one of ordinary skill, 5) the level of predictability in the art, 6) the amount of direction provided by the inventor, 7) the existence of working examples, and 8) the quantity of experimentation needed to make or use the invention based on the content of the disclosure. In re Wands, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988).

1) The breadth of the claims: The instant claims encompass many compounds with various substitutions.

R_3 is selected from the group consisting of:

$-R_4$,

$-X-R_4$,

$-X-Y-R_4$, and

$-X-R_5$;

X is selected from the group consisting of alkylene, alkenylene, alkynylene, arylene, heteroarylene, and heterocyclylene, wherein the alkylene, alkenylene, and alkynylene groups can be optionally interrupted or terminated with arylene, heteroarylene, or heterocyclylene, and optionally interrupted by one or more -O- groups;

Y is selected from the group consisting of:

-O-,

$-S(O)_{0-2}-$,

$-S(O)_2-N(R_8)-$,

$-C(R_6)-$,

$-C(R_6)-O-$,

-O-C(R_6)-,

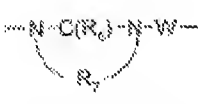
-O-C(O)-O-,

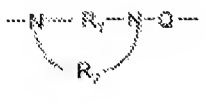
-N(R_6)-Q-,

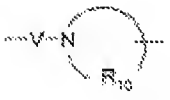
-C(R_6)-N(R_6)-,

-O-C(R_6)-N(R_6)-,

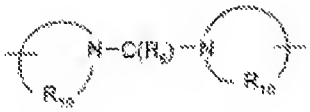
-C(R_6)-N(OR_6)-,







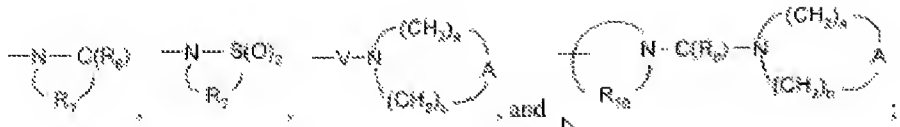
, and



;

R_4 is selected from the group consisting of hydrogen, alkyl, alkenyl, alkynyl, aryl, arylalkylenyl, aryloxyalkylenyl, alkylarylenyl, heteroaryl, heteroarylalkylenyl, heteroaryloxyalkylenyl, alkylheteroarylenyl, and heterocyclyl, wherein the alkyl, alkenyl, alkynyl aryl, arylalkylenyl, aryloxyalkylenyl, alkylarylenyl, heteroaryl, heteroarylalkylenyl, heteroaryloxyalkylenyl, alkylheteroarylenyl, and heterocyclyl groups can be unsubstituted or substituted by one or more substituents independently selected from the group consisting of alkyl, alkoxy, hydroxyalkyl, haloalkyl, haloalkoxy, halogen, nitro, hydroxy, mercapto, cyano, aryl, aryloxy, arylalkylenyloxy, heteroaryl, heteroaryloxy, heteroarylalkylenyloxy, heterocyclyl, amino, alkylamino, dialkylamino, (dialkylamino)alkylenyloxy, and in the case of alkyl, alkenyl, alkynyl, and heterocyclyl, oxo;

R_5 is selected from the group consisting of



, and ;

R_5 is selected from the group consisting of =O and =S;

R_7 is C_{2-7} alkylene;

R_8 is selected from the group consisting of hydrogen, alkyl, alkoxyalkylenyl, and arylalkylenyl;

R_9 is selected from the group consisting of hydrogen and alkyl;

R_{10} is C_{3-8} alkylene;

A is selected from the group consisting of -O-, -C(O)-, $-CH_2-$, $-S(O)_{0-2}-$, and $-N(R_4)-$;

A' is selected from the group consisting of -O-, -C(O)-, $-CH_2-$, $-S(O)_{0-2}-$, $-N(R_4)-$, and $-N(Q-R_4)-$;

Q is selected from the group consisting of a bond, $-C(R_6)-$, $-C(R_6)-C(R_6)-$, $-S(O)_2-$, $-C(R_6)-N(R_8)-W-$, $-S(O)_2-N(R_8)-$, $-C(R_6)-O-$, and $-C(R_6)-N(OR_9)-$;

V is selected from the group consisting of $-C(R_6)-$, $-O-C(R_6)-$, $-N(R_8)-C(R_6)-$, and $-S(O)_2-$;

W is selected from the group consisting of a bond, -C(O)-, and $-S(O)_2-$;

a and b are independently integers from 1 to 6 with the proviso that a + b is ≤ 7;

2) The nature of the invention: The invention is a (highly) substituted compound that is useful as a pharmaceutical.

3) The state of the prior art: Regarding how to use:-The state of the prior art is that the drugs and the enzymes react in a lock and key mechanism and the structure of the compound has to be specific. Even a difference of a methyl group verses a hydrogen changes the properties altogether. A good example is a theophylline verses caffeine. They differ by just a methyl group but one of them has a pharmaceutical use as a bronchodilator. There is no absolute predictability and no established correlation between the different substitutions on a core that they would all behave in the exact same way. The existence of these obstacles establishes that the contemporary knowledge in the art would prevent one of ordinary skill in the art from accepting any therapeutic regimen on its face.
How to make :-
As stated in the preface to a recent treatise:
"Most non-chemists would probably be horrified if they wereto learn how many attempted syntheses fail, and how inefficient research chemists are. The ratio of successful to unsuccessful chemical experiments in a normal research laboratory is far below unity, and synthetic research chemists, in the same way as most scientists, spend most of their time working out what went

wrong, and why. Despite the many pitfalls lurking in organic synthesis, most organic chemistry textbooks and research articles do give the impression that organic reactions just proceed smoothly and that the total synthesis of complex natural products, for instance, is maybe a labor-intensive but otherwise undemanding task. In fact, most syntheses of structurally complex natural products are the result of several years of hard work by a team of chemists, with almost every step requiring careful optimization. The final synthesis usually looks quite different from that originally planned, because of unexpected difficulties encountered in the initially chosen synthetic sequence. Only the seasoned practitioner who has experienced for himself the many failures and frustrations which the development (sometimes even the repetition) of a synthesis usually implies will be able to appraise such work .....Chemists tend not to publish negative results, because these are, as opposed to positive results, never definite (and far too copious) ....." Dorwald F. A.
Side Reactions in Organic Synthesis, 2005, Wiley: VCH, Weinheim pg. IX of Preface

4) The level of one of ordinary skill: The ordinary artisan is highly skilled.

5) The level of predictability in the art: It is noted that the pharmaceutical art is unpredictable , requiring each embodiment to be individually assessed for physiological activity. In re Fisher, 427 F. 2d 833, 166 USPQ 18(CCPA 1970) indicates that the more unpredictable an area is, the more specific enablement is necessary in order to satisfy the statue. The level of unpredictability is in the art is very high. The compounds which differ by a methyl group also show different properties, for e.g. theophylline and caffeine. One of them is a bronchodilator and they differ only by a methyl group.
Ex parte DIAMOND, 123 USPQ 167 (Bd. Pat. App. & Int. 1959) where the examiner was affirmed for a scope of enablement rejection, and the court stated:

Scope of claims should not be unduly extensive in chemical fields where applicability is highly speculative or not explored; subject matter which relies upon prediction for its support is unpatentable.
Specification contains 23 specific examples, but they are to preparation of relatively simple compounds; this is relatively meager and non representative disclosure to support claims embracing millions of compounds.
Applicant may not preempt unduly large field by expedient of making broad prophetic statements in specification and claims unless accuracy of such statements is sufficiently supported by well established chemical principles or by sufficient number of examples.
"The term 'substituted' without modification or restriction includes all compounds wherein one or more of the atoms or radicals of the original compound have been replaced by one or more other atoms or radicals. Without any limitation on the character or number of substituents it becomes apparent that the quoted term may be considered inclusive of almost any possible substance and the claims under consideration are either of unlimited or indeterminate scope. We are of the opinion that the reasoning of the courts in Schering Corp. v. Gilbert, 68 USPQ 84, and Hercules Powder Co. v. Rohm & Haas, 70 USPQ 297, is controlling."
embrace millions of compounds. It should also be observed that appellant is working in a field where little prediction is possible and this Board has on several occasions held that the scope of

claims should not be unduly extensive in fields where applicability is highly speculative or not explored and that subject matter which relies upon prediction for its support is unpatentable

6) The amount of direction provided by the inventor: The inventor provides very little direction in the instant specification. There are few examples with the R2 being a alkyloxyalkyl or an alkyl group. As can be seen from the breadth of the claim there are many variations at the R2 position.

7) The existence of working examples: The instant specification has many examples but it is limited to only a small subclass of the variables claimed. An example corresponding to each class is not provided.

8) The quantity of experimentation needed to make or use the invention based on the content of the disclosure: Since there are no working examples corresponding to the different classes and different classes are known to have different properties, the amount of experimentation is very high and burdensome.

Taking the above eight factors into consideration, it is not seen where the instant specification enables the ordinary artisan to make and/or use the instantly claimed invention.

Genetech Inc Vs Nova Nordisk 42 USPQ 2d 1001.

"A patent is not a hunting license. It is not a reward for search but compensation for its successful conclusion and patent protection is granted in return for an enabling disclosure of an invention , not for vague intimations of general ideas that may or may not be workable."

MPEP 2164.01(a) states, "A conclusion of lack of enablement means that,

based on the evidence regarding each of the above factors, the specification, at the time the application was flied, would not have taught one skilled in the art how to make and/or use the full scope of the claimed invention without undue experimentation. In re Wright, 999 F.2d 1557,1562, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993)." That conclusion is clearly justified here. Thus, undue

experimentation will be required to practice Applicants' invention.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

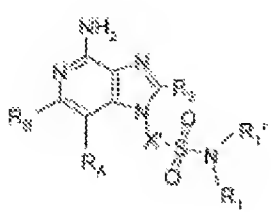
Claims 2, 4, 5-6, 12, 14-16, 18, 20-21, 23-25, 39-54, 61, 63, and 65 are rejected under 35 U.S.C. 103(a) as being obvious over WO 2004058759, US 7091214 , US 6525064, WO2005076783, WO 2005/051324, WO 2005/051317 (same assignees)

The applied reference has a common assignee with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art only under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 103(a) might be overcome by: (1) a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not an invention "by another"; (2) a showing of a date of invention for the claimed subject matter of the application which corresponds to subject matter disclosed but not claimed in the reference, prior to the effective U.S. filing date of the reference under 37 CFR 1.131; or (3) an oath or declaration under 37 CFR 1.130 stating that the application and reference are currently owned by the same party and that the inventor named in the application is the prior inventor under 35 U.S.C. 104, together with a terminal disclaimer in accordance with 37 CFR 1.321(c). This rejection might also be overcome by showing that the

reference is disqualified under 35 U.S.C. 103(c) as prior art in a rejection under 35 U.S.C. 103(a). See MPEP § 706.02(l)(1) and § 706.02(l)(2).

Applicants compounds are drawn to the formula

.



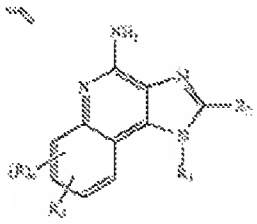
(Ia)

wherein Ra and Rb form a ring, R1 and R1' are

are H, alkyl, alkyl aryl, cycloakyl or are combined to form a morpholine or piperidine,

Scope & Content of Prior Art MPEP 2141.01

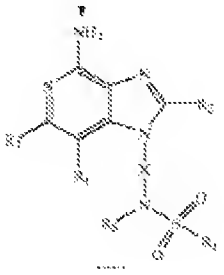
The prior art US 7091214 disclos es similar core and with similar substitutents. (corresponds to WO



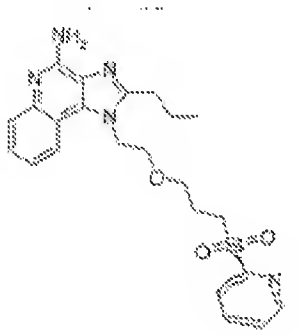
2004058759, US 200601111387)

See formula XV, column 48, Column 197, eg 368.

US 6525064 teaches similar compounds but with aminosulfomide instead of the sulfonamide.

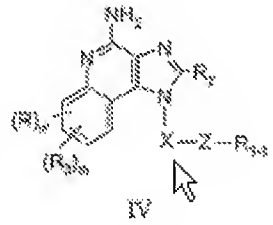


WO2005076783, teaches compounds with the same core , and compounds such as

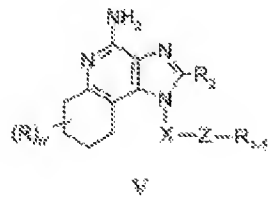


.see page 105.

WO 2005/051324, teaches



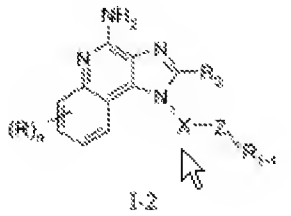
IV



V

which is the same core but with the ZR1-1 to be various functional groups such as carboxyamide, urea, and also sulfonamide (eg 8 page 128, 124).

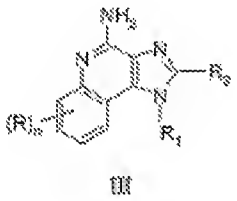
WO 2005/051317 teaches the compounds of the formula



I-2

with the ZR1-1 to be a carboxyamide instead of the sulfonamide.

WO200518555 teaches compounds of the formula



III

see page 43, wherein L is -NHSO2 instead of the –-SO2NH- of the claimed application.

Difference between Prior Art and the claims MPEP 2141.02

Very similar compounds are disclosed. It should be noted none of the species have the R2 substitutent corresponding to the R2 of the applicants.

The same core is taught with various functional group including reverse sulfonamides are taught.

Prima Facie Obviousness , Rational and Motivation MPEP 2142-2413

With so many different functional groups and the same core being taught for compounds which have the same activity, one of skill in the art would be motivated to modify the reverse sulfonamides to the sulfonamides to obtain the compounds of the invention and expect the properties to be retained as there is a lot of teaching that various different functional groups work and retain their activity. In the absence of unexpected results the compounds are obvious over those of the prior art.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 2, 4, 5-6, 12, 14-16, 18, 20-21, 23-25, 39-54, 61, 63, and 65 rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1 of U.S. Patent No. 7091214 in view of , US 6525064, WO2005076783, WO 2005/051324, WO 2005/051317 (same assignees) . Although the conflicting claims are not identical, they are not

patentably distinct from each other because the art suggests making small modifications in the functional group or in the substituents on the carbocyclic ring does not change the activity. See the 103 rejection above.

Claims 2, 4, 5-6, 12, 14-16, 18, 20-21, 23-25, 39-54, 61, 63, and 65 provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claim s 1-6 of copending Application No. 11/275553. Although the conflicting claims are not identical, they are not patentably distinct from each other because the claims are drawn to the reverse sulfonamides and in view of all the various references cited above , it is obvious to modify the functional group to make them sulfonamides and still expect the properties to remain the same.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Conclusion

Claims 2, 4, 5-6, 12, 14-16, 18, 20-21, 23-25, 39-54, 61, 63, and 65 are rejected.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Rita J. Desai whose telephone number is 571-272-0684. The examiner can normally be reached on Monday - Friday, flex time..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Janet Andres can be reached on 571-272-0867. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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/Rita J. Desai/
Primary Examiner, Art Unit 1625

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